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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/528,914 | 01/05/2006 | Margaret Han Dugan | ON/4-32695A | 6406 |

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

| EXAMINER | |
|---|---|
| SZNAIDMAN, MARCOS L | |
| ART UNIT | PAPER NUMBER |
| 1612 | |

| MAIL DATE | DELIVERY MODE |
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| 11/12/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/528,914 | DUGAN ET AL. | |
| | Examiner | Art Unit | |
| | MARCOS SZNAIDMAN | 1612 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This office action is in response to applicant's reply filed on July 24, 2008.

### *Status of Claims*

Claims 1- 12 are currently pending and are the subject of this office action.

Claims 7-12 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Election has been treated as an election without traverse in the reply filed on December 5, 2007.

Claims 1-6 are currently under examination.

Species being examined: PTK 787 as the 4-pyridylmethyl-phtalazine derivative of formula I.

### *Priority*

The present application is a 371 of PCT/EP03/210578 filed on 09/23/2003, and claims priority to provisional application No. 60/413,176 filed on 09/24/2002.

### *Response to Arguments*

This is in response to applicant's arguments, filed on July 24, 2008.

***Claims rejected under 35 USC 112, first paragraph (enablement).***

Applicant's arguments have been fully considered and they are persuasive.

Rejection under 35 USC 112, first paragraph (enablement) is withdrawn.

***Claims rejected under 35 USC 103 (a)***

Applicant's arguments have been fully considered and are persuasive. Therefore the rejection is withdrawn.

However, upon further consideration, a new ground(s) of rejection is made in view of new prior art.

A new USC 103 (a) rejection is applied.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raza et. al. (Blood (2001) 98: 958-965) and Canepa et. al. (British Journal of Haematology (2001) 115:313-315) in view of Drevs et. al. (Cancer Research (2000) 60:4819-4824).

Claims 1-3 and 5 recite a method of treating myelodysplastic syndromes (MDS) comprising administering a therapeutically effective amount of PTK787 (species elected) to a warm blooded animal (human in claim 5) in need thereof.

For claims 1-3 and 5, Raza et. al. teach a method of treating MDS with thalidomide (see abstract and introduction). Canepa et. al. further teach that

thalidomide is a VEGF inhibitor (see page 313, left column, last line through right column, fourth line).

Neither Raza et. al. nor Canepa et. al. teach the treatment of MDS with PTK787. However, Drevs et. al. teach that PTK787 is an inhibitor of VEGF receptor (see abstract, line 5). Drevs et. al. also teach that PTK787 is used for the treatment of renal cancer in vivo in a murine model.

Since Raza et. al. teach a method of treating MDS with thalidomide (a VEGF inhibitor according to Canepa et. al.), and since Drevs et. al. teach that PTK787 is a VEGF inhibitor, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any VEGF inhibitor including thalidomide) for another (PTK787) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claims 1-3 and 5, with a reasonable expectation of success.

Claim 6 further limits claim 1, wherein the total daily dosage of PTK787 is applied to the warm blooded animal by administration of two separate units comprising the same or different amounts of PTK787.

For claim 6, Drevs further teaches that PTK787 can be administered once daily (see page 4820, under administration of drugs). Drevs is silent regarding the number of units, however it's within the capability of the ordinary artisan to optimize the dosage for a particular patient and optimize dosage amounts based on the observed clinical

effectiveness, thus resulting in the practice of claim 6 with a reasonable expectation of success.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Raza et. al. (Blood (2001) 98: 958-965) and Canepa et. al. (British Journal of Haematology (2001) 115:313-315) in view of Drevs et. al. (Cancer Research (2000) 60:4819-4824) as applied to claims 1-3 and 5-6 above, in further view of Calabresi et. al. (US 6,429,224)

Claim 4 further limits claim 1, wherein the disease is resistant to conventional chemotherapy.

Raza et. al. and Canepa et. al. in view of Drevs et. al. teach all the limitations of claim 4, except for the disease being resistant to conventional therapy.

However, Calabresi et. al. teach that myelodysplastic syndrome cells can be resistant to drugs (see column 9, lines 26-27).

Thus, it would have been *prima facie* obvious at the time the invention was made to modify the patient population as taught by Raza et. al. in order to include patients having MDS which are resistant to conventionally therapies in further view of Calabresi et al. One would have been motivated to do so because as taught by Calabresi et al., some patients undergoing treatment for MDS are resistant to conventional therapies. Thus, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art, to further treat MDS patients that were resistant to conventional chemotherapy with PTK787, thus resulting in the practice of claim 4 with a reasonable expectation of success.

***Conclusion***

No claims are allowed.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
October 30, 2008

/Brandon J Fetterolf/

Primary Examiner, Art Unit 1642